Complete Summary

GUIDELINE TITLE

Carrier screening for thalassemia and hemoglobinopathies in Canada.

BIBLIOGRAPHIC SOURCE(S)

Langlois S, Ford JC, Chitayat D, Desilets VA, Farrell SA, Geraghty M, Nelson T, Nikkel SM, Shugar A, Skidmore D, Allen VM, Audibert F, Blight C, Gagnon A, Johnson JA, Wilson RD, Wyatt P. Carrier screening for thalassemia and hemoglobinopathies in Canada. J Obstet Gynaecol Can 2008 Oct;30(10):950-9. [28 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Autosomal recessive conditions, such as:

- Thalassemia
- Hemoglobinopathies
- Sickle cell disorders

GUIDELINE CATEGORY

Counseling
Prevention

Risk Assessment
Screening

CLINICAL SPECIALTY

Hematology
Medical Genetics
Obstetrics and Gynecology
Pediatrics

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

- To provide recommendations to physicians, midwives, genetic counsellors, and clinical laboratory scientists involved in pre-conceptional or prenatal care regarding carrier screening for thalassemia and hemoglobinopathies (e.g., sickle cell anemia and other qualitative hemoglobin disorders)
- To determine the populations to be screened and the appropriate tests to offer to minimize practice variations across Canada

TARGET POPULATION

Patient or her partner at risk for thalassemia and/or hemoglobinopathy

INTERVENTIONS AND PRACTICES CONSIDERED

Screening/Risk Assessment

1. Risk assessment
2. Carrier screening
    - Complete blood count (CBC)
    - Hemoglobin electrophoresis
    - Hemoglobin high performance liquid chromatography (HPLC)
    - Quantitation of HbA2 and HbF
    - H body staining (brilliant cresyl blue)
    - Serum ferritin
3. Partner screening (when indicated)
    - CBC
    - Hemoglobin electrophoresis (HPLC)
    - Quantitation of HbA2 and HbF
    - H body staining (brilliant cresyl blue)
4. Genetic counseling
5. Prenatal diagnosis
    - DNA analysis
    - Serial detailed fetal ultrasound

MAJOR OUTCOMES CONSIDERED

- Completion of pregnancy
- Maternal and fetal perinatal morbidity and mortality
- Risk of thalassemia or hemoglobinopathy

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The Medline database was searched for relevant articles published between 1986 and 2007 on carrier screening for thalassemia and hemoglobinopathies. Key textbooks were also reviewed.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Quality of Evidence Assessment*

I: Evidence obtained from at least one properly designed randomized controlled trial.

II-1: Evidence obtained from well-designed controlled trials without randomization.

II-2: Evidence obtained from well-designed cohort (prospective or retrospective) or case–control analytic studies, preferably from more than one center or research group.

II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category

III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

* Adapted from the Evaluation of Evidence criteria described in the Canadian Task Force on Preventive Health Care.

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The evidence collected from the Medline search was reviewed by the Prenatal Diagnosis Committee of the Canadian College of Medical Geneticists (CCMG) and the Genetics Committee of the Society of Obstetricians and Gynaecologists of Canada (SOGC).

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Classification of Recommendations*

A. There is good evidence to recommend the clinical preventive action

B. There is fair evidence to recommend the clinical preventive action

C. The existing evidence is conflicting and does not allow to make a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making

D. There is fair evidence to recommend against the clinical preventive action

E. There is good evidence to recommend against the clinical preventive action

L. There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making

* Adapted from the Classification of Recommendations criteria described in the Canadian Task Force on Preventive Health Care.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

This clinical practice guideline has been prepared by the Genetics Committee of the Society of Obstetricians and Gynaecologists of Canada (SOGC) and the Prenatal Diagnosis Committee of the Canadian College of Medical Geneticists (CCMG) and reviewed and approved by the Executive and Council of the SOGC and the Board of Directors of the CCMG.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The quality of evidence (I-III) and classification of recommendations (A-E) are defined at the end of the "Major Recommendations."

1. Carrier screening for thalassemia and hemoglobinopathies should be offered to a woman if she and/or her partner are identified as belonging to an ethnic population whose members are at higher risk of being carriers. Ideally, this screening should be done pre-conceptionally or as early as possible in the pregnancy. **(II-2A)**
2. Screening should consist of a complete blood count, as well as hemoglobin electrophoresis or hemoglobin high performance liquid chromatography. This investigation should include quantitation of HbA2 and HbF. In addition, if there is microcytosis (mean cellular volume < 80 fL) and/or hypochromia (mean cellular hemoglobin < 27 pg) in the presence of a normal hemoglobin electrophoresis or high performance liquid chromatography the patient should be investigated with a brilliant cresyl blue stained blood smear to identify H bodies. A serum ferritin (to exclude iron deficiency anemia) should be performed simultaneously. **(III-A)**
3. If a woman's initial screening is abnormal (e.g., showing microcytosis or hypochromia with or without an elevated HbA2, or a variant Hb on electrophoresis or high performance liquid chromatography) then screening of the partner should be performed. This would include a complete blood count as well as hemoglobin electrophoresis or high performance liquid chromatography (HPLC), HbA2 and HbF quantitation, and H body staining. **(III-A)**
4. If both partners are found to be carriers of thalassemia or an Hb variant, or of a combination of thalassemia and a hemoglobin variant, they should be referred for genetic counselling. Ideally, this should be prior to conception, or as early as possible in the pregnancy. Additional molecular studies may be required to clarify the carrier status of the parents and thus the risk to the fetus. **(II-3A)**
5. Prenatal diagnosis should be offered to the pregnant woman/couple at risk for having a fetus affected with a clinically significant thalassemia or hemoglobinopathy. Prenatal diagnosis should be performed with the patient's informed consent. If prenatal diagnosis is declined, testing of the child should be done to allow early diagnosis and referral to a pediatric hematology centre, if indicated. **(II-3A)**

6. Prenatal diagnosis by DNA analysis can be performed using cells obtained by chorionic villus sampling or amniocentesis. Alternatively for those who decline invasive testing and are at risk of hemoglobin Bart's hydrops fetalis (four-gene deletion alpha-thalassemia), serial detailed fetal ultrasound for assessment of the fetal cardiothoracic ratio (normal < 0.5) should be done in a centre that has experience conducting these assessments for early identification of an affected fetus. If an abnormality is detected, a referral to a tertiary care centre is recommended for further assessment and counselling. Confirmatory studies by DNA analysis of amniocytes should be done if a termination of pregnancy is being considered. **(II-3A)**
7. The finding of hydrops fetalis on ultrasound in the second or third trimester in women with an ethnic background that has an increased risk of alpha thalassemia should prompt immediate investigation of the pregnant patient and her partner to determine their carrier status for alpha-thalassemia. **(III-A)**

Definitions:

Quality of Evidence Assessment*

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Classification of Recommendations**

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*The quality of evidence reported in these guidelines has been adapted from The Evaluation of Evidence criteria described in the Canadian Task Force on Preventive Health Care.

**Recommendations included in these guidelines have been adapted from the Classification of Recommendations criteria described in the Canadian Task Force on Preventive Health Care.

CLINICAL ALGORITHM(S)

An "Approach to Screening" algorithm is provided in the original guideline document.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Screening of individuals at increased risk of being carriers for thalassemia and hemoglobinopathies can identify couples with a 25% risk of having a pregnancy with a significant genetic disorder for which prenatal diagnosis is possible. Ideally, screening should be done pre-conceptionally.

POTENTIAL HARMS

For a significant proportion of patients, the screening will occur during the pregnancy, and the time constraint for obtaining screening results may result in psychological distress.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This document reflects emerging clinical and scientific advances on the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed. Local institutions can dictate amendments to these opinions. They should be well documented if modified at the local level.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2008 Oct

GUIDELINE DEVELOPER(S)

Society of Obstetricians and Gynaecologists of Canada - Medical Specialty Society

SOURCE(S) OF FUNDING

Society of Obstetricians and Gynaecologists of Canada

GUIDELINE COMMITTEE

Genetics Committee of the Society of Obstetricians and Gynaecologists of Canada
Prenatal Diagnosis Committee of the Canadian College of Medical Geneticists

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Society of Obstetricians and Gynaecologists of Canada Web site.

Print copies: Available from the Society of Obstetricians and Gynaecologists of Canada, La société des obstétriciens et gynécologues du Canada (SOGC) 780 promenade Echo Drive Ottawa, ON K1S 5R7 (Canada); Phone: 1-800-561-2416

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI Institute on March 3, 2009. The information was verified by the guideline developer on March 13, 2009.

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